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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,067	12/03/2003	Kenneth F. Buechler	071949-5604	7956

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FOLEY & LARDNER LLP
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER	
JUNG, UNSU	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,067	BUECHLER ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-44* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-44 are pending.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-31, drawn to a method of predicting a risk of one or more future clinical outcomes for a subject suffering from a vascular disease, classified in class 435, subclass 7.1, for example.

II. Claims 32-44, drawn to a method of diagnosing atherosclerosis in a subject, classified in class 435, subclass 13, for example.

3. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are independent and patentably distinct. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the method of Group I involves a step of correlating a presence or amount of thrombus precursor protein to a risk of one or more clinical outcomes for a subject suffering from a vascular disease, which is not required by the method of Group II. The method of Group II involves a step of correlating a presence or amount of monocyte chemoattractant protein-1 to the presence or absence of atherosclerosis in the subject, which is not required by the method of Group I. Therefore, the methods of Groups I and II have different designs, modes of operation, and effects.

4. Because these inventions are independent or distinct for the reasons given above and searches for one group are not required by the others, there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Election of Species within Group I

5. This application contains claims directed to the following patentably distinct species of the claimed invention I. If, Group I is elected, the applicant is required to elect one species (indicated by letters) from each of the following lists of species. For the species having subspecies (indicated by numbers), applicant is further required to elect one subspecies.

List I: Vascular Diseases (claims 2, 3, 9)

a. acute coronary syndrome
b. atherosclerosis
c. ischemic stroke
d. intracerebral hemorrhage
e. subarachnoid hemorrhage
f. transient ischemic attack
g. systolic dysfunction
h. diastolic dysfunction
i. aneurysm
j. aortic dissections
k. myocardial ischemia
l. angina pectoris
m. myocardial infarction
n. congestive heart failure
o. dilated congestive cardiomyopathy
p. hypertrophic cardiomyopathy

q. restrictive cardiomyopathy
r. cor pulmonale,
s. arrhythmia
t. valvular heart disease
u. endocarditis
v. pulmonary embolism
w. venous thrombosis
x. peripheral vascular disease.

List II: Future Clinical Outcomes (claim 4)

a. death
b. nonfatal myocardial infarction
c. recurrent ischemia requiring rehospitalization
d. recurrent ischemia requiring urgent revascularization
e. congestive heart failure

List III: Subject-Derived Markers (claims 12-23, 30, and 31)

a. annexin V
b. B-type natriuretic peptide,
c. β-enolase
d. free cardiac troponin I
e. complexed cardiac troponin I
f. free and complexed cardiac troponin I
g. free cardiac troponin T
h. complexed cardiac troponin T
i. free and complexed cardiac troponin T
j. creatine kinase-MB
k. glycogen phosphorylase-BB
l. heart-type fatty acid binding protein
m. phosphoglyceric acid mutase-M
n. S-100ao
o. adenylate kinase
p. brain-derived neurotrophic factor
q. calbindin-D
r. creatine kinase-BB
s. glial fibrillary acidic protein
t. lactate dehydrogenase
u. myelin basic protein
v. neural cell adhesion molecule (NCAM)
w. c-tau

x. neuropeptide Y
y. neuron-specific enolase
z. neurotrophin-3
aa. proteolipid protein
bb. S-100/3
cc. Thrombomodulin
dd. protein kinase C γ
ee. atrial natriuretic peptide (ANP)
ff. pro-ANP
gg. B-type natriuretic peptide (BNP)
hh. NT-pro BNP
ii. pro-BNP C-type natriuretic peptide
jj. urotensin II
kk. arginine vasopressin
ll. aldosterone
mm. angiotensin I
nn. angiotensin II
oo. angiotensin III
bradykinin
pp. calcitonin
qq. procalcitonin
rr. calcitonin gene related peptide
ss. adrenomedullin
tt. calcyphosine
uu. endothelin-2
vv. endothelin-3
ww. rennin
xx. urodilatin
yy. acute phase reactants
zz. cell adhesion molecules
aaa. C-reactive protein
bbb. Interleukins
ccc. interleukin-1 receptor agonist
ddd. monocyte chemoattractant protein-1
eee. caspase-3
fff. lipocalin-type prostaglandin D synthase
ggg. mast cell tryptase
hhh. eosinophil cationic protein
iii. KL-6
jjj. Haptoglobin
kkk. tumor necrosis factor α
lll. tumor necrosis factor β
mmm. Fas ligand
nnn. soluble Fas (Apo-1)

ooo. TRAIL
ppp. TWEAK
qqq. Fibronectin
rrr. macrophage migration inhibitory factor (MIF)
sss. vascular endothelial growth factor (VEGF)
ttt. myeloperoxidase
uuu. caspase-3
vvv. cathepsin D
www. a-spectrin
xxx. plasmin
yyy. fibrinogen
zzz. D-dimer
aaaa. β-thromboglobulin
bbbb. platelet factor 4
cccc. fibrinopeptide A
dddd. platelet-derived growth factor
eeee. prothrombin fragment 1+2
ffff. plasmin-α2-antiplasmin complex
gggg. thrombin-antithrombin III complex
hhhh. P-selectin
iiii. thrombin
jjjj. von Willebrand factor
kkkk. tissue factor

List II: Correlating Step (claims 5-10 and 27-29)

a. correlating step comprises determining the concentration of thrombus precursor protein in said sample, and comparing said concentration to a threshold concentration, wherein a concentration of thrombus precursor protein less than said threshold concentration is indicative, of a first risk of said one or more clinical outcomes and a concentration of thrombus precursor protein greater than said threshold concentration is indicative of a second risk of one or more clinical outcomes (claims 5-10 and 27)

threshold concentration
(1) ROC curve area
(2) odds ratio
(3) hazard ratio

b. correlating step comprises determining the concentration of thrombus precursor protein and said one or more other subject-derived markers, calculating a single index value based on each concentration, and comparing the index value to a threshold level (claim 28)

c. determining a temporal change in thrombus precursor protein concentration, and wherein said temporal change is used in the correlating step (claim 29)

The species are independent or distinct because each species of molecules has patentably distinct chemical structure and biological function and each species of vascular disease and clinical outcomes has patentably distinct pathology. Further, each species of correlation step involves patentably distinct steps to determine the risk of clinical outcomes.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 11, and 24-26 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Election of Species within Group II

6. This application contains claims directed to the following patentably distinct species of the claimed invention II. If, Group II is elected, the applicant is required to elect one species (indicated by letters) from each of the following lists of species. For the species having subspecies (indicated by numbers), applicant is further required to elect one subspecies.

List I: Risk Factors (claims 34)

a. sex
b. age
c. a diagnosis of diabetes
d. a diagnosis of hypertension
e. past tobacco use
f. a cholesterol concentration
g. family history of atherosclerosis

List II: Subject-Derived Markers (claims 12-23, 30, and 31)

a. monocyte chemoattractant protein-1
b. markers related to myocardial injury markers
c. specific markers of neural tissue injury
d. markers related to blood pressure regulation
e. markers related to coagulation and hemostasis
f. markers related to inflammation
g. markers related to apoptosis

The species are independent or distinct because each species of molecules has patentably distinct chemical structure and biological function and each species of vascular disease and clinical outcomes has patentably distinct pathology. Further, each species of correlation step involves patentably distinct steps to determine the risk of clinical outcomes.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 32, 33, 35-40, and 42-44 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

7. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Unsu Jung, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 09/01/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600